

MSK.P-026-2
Patent Application

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Houghton, et al.	Confirmation No.:	3599
Serial No.:	09/627,694	Examiner:	A. Harris
Filed:	28 July 2000	Art Unit:	1642
For:	Method and Compositions for Stimulation of an Immune Response to Differentiation Antigen Induced by Altered Differentiation Antigen		

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RESPONSE TO FINAL REJECTION

This is in response to the Official Action mailed April 22, 2002 for the above-captioned application. Reconsideration of the application in view of the remarks herein is respectfully requested.

Claims 31, 33-37 and 40 are pending. The Examiner rejected claims 31 and 33 as obvious over Houghton, et al. in view of Ausubel, et al. Applicants respectfully submit that the claims are not obvious over the cited combination of references.

On May 7, 2002, Applicants' Attorneys met with Examiner Harris to discuss the Examiner's rejection under 35 USC §103 of Claims 31 and 33 based on the Houghton and Ausubel references. The Bouchard reference (Bouchard et al., *J. Exp. Med.* 169: 2029-42 (1989)) was also discussed. Applicants thank the Examiner for taking the time for the personal interview. This paper will serve as a summary of the interview.

In the Office Action, the Examiner made the argument that Applicants' arguments are not commensurate with the scope of the claims. Applicants respectfully submit that the Examiner's argument misses the point. The correct legal standard is that the Examiner must look to all of the teachings of the art to see what is suggested and not just pick and choose among the teachings to support the rejection. The references are teachings in the art that indicate how a person skilled in the art would view issues of motivation and likelihood of success.

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Applicants respectfully submit that one of ordinary skill in the art would have no motivation to combine the Houghton and Ausubel references. As Applicants' Attorney argued at the interview, Ausubel provides no motivation or suggestion to modify the teaching of Houghton to use insect cells instead of mouse cells, nor even a suggestion that insect cell lines would be expected to provide appropriate processing of melanosomal proteins to provide for the studies that are the subject of Houghton. As for Houghton, the overall goal was to study the recognition of autoantigens by patients with melanoma, and the preparation of gp75 was performed so that the testing could be done to compare gp75 expressed in mouse cells with gp75 expressed in human cells. Once the initial testing was done, there was no reason to make more of the gp75; the experiment was complete and the results were conclusive. Houghton provides no motivation or suggestion to make more gp75, much less to seek more efficient or different methods for preparing gp75 using a different host cell type.

In the Office Action, the Examiner asserted that Ausubel teaches a "great likelihood of obtaining biologically active products from such methods and host cells due to the baculovirus' efficient promoter strategy and the high infection rate of insect host cells." At the interview, Applicants Attorney argued that what the reference actually teaches is a likelihood that if a protein is expressed, it will happen in a reasonable yield. In fact, Ausubel includes a teaching that actual expression may not occur.

Ausubel makes it clear that baculoviruses may not work for producing all proteins. On page 16.8.3, second column, towards the bottom, Ausubel provides as one of the steps for overproducing proteins using the baculoviral expression system: "5. Determine whether the potential recombinant viruses express the protein of interest." On page 16.11.3, first paragraph, Ausubel recommends that the recombinant virus be screened for its ability to produce the protein of interest, and that the screening should be individually tailored to the properties of the protein being overproduced and the availability of detection reagents. Ausubel does not contemplate that the baculovirus expression system will work for all proteins, and Ausubel recognizes that experimentation will be needed to determine whether a particular protein of interest could be produced using this system. Ausubel suggests ways to optimize for protein production if the

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protein production is possible using the system, but Ausubel provides no motivation or suggestion that insect cell lines would be expected to produce melanosomal proteins as discussed in Houghton.

Additionally, on page 16.11.5 under Determining Time Course of Maximum Protein Production Ausubel states that "because individual proteins display differences in their stability in insect cells, it is recommended that the time course of protein accumulation be charted for each protein expressed using this system." This further emphasizes that baculoviruses would not be suitable for production of all proteins and that a significant amount of experimentation may be required to determine whether the baculovirus system would be suitable for production of a particular protein. Therefore, Applicants respectfully submit that, contrary to the Examiner's assertion, Ausubel does not teach a great likelihood of obtaining biologically active products, but rather teaches that the system may not work for all proteins and experimentation will be necessary to determine if the system will work for a particular protein.

Also, during the interview, Applicants' Attorney pointed out that unexpected results were obtained by Applicants' invention. Houghton mentions expression of human gp75 in mouse fibroblasts and cites to a reference that describes the use of methods as described in Bouchard, which describes expression of human tyrosinase cDNA in mouse fibroblasts. Applicants' Attorney pointed out that Bouchard concerns a different protein and teaches concern about whether melanosomal proteins are expressable at all in mammalian cells which lack melanosomes. In the present invention, Applicants have found that such proteins are expressable not only in mammalian cells, but also insect cells to produce a differentiation antigen, and that this differentiation antigen is different than the autoantigen, such that the differentiation antigen can be introduced into a tumor-bearing host to break the tolerance to the autoantigen and stimulate an immune response to the tumor.

Finally, in the Office Action the Examiner asserted that "one of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because it is art known that sources of altered antigen can induce effective immune responses, such as tumor rejection." During the interview, Applicants' Attorney argued that this is the Applicants'

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discovery, and that if this statement is true, the Examiner should provide a reference. The Examiner agreed that a reference should be required to support her assertion that it is art known that sources of altered antigen can induce effective immune responses, such as tumor rejection.

In conclusion, Applicants assert that none of the references cited by the Examiner contain a suggestion or motivation for combining the teachings of the references. Ausubel is a basic reference teaching how insect cells may be used to express some antigens if such expression could occur. Houghton teaches the comparison of gp75 as expressed in human cells with gp75 as expressed in mouse cells for the purpose of studying whether the antigens would be recognized in patients with melanoma. Houghton provides no motivation or suggestion to seek more efficient or different methods for preparing gp75. Ausubel provides no motivation or suggestion to modify the teaching of Houghton to use insect cells instead of mouse cells. Further, Ausubel provides no suggestion that insect cell lines would be expected to produce melanosomal proteins that were the subject of the studies in Houghton. Additionally, unexpected results were obtained in Applicants' invention. Therefore, one skilled in the art would have no motivation to combine the references, nor would Applicants' invention be obvious in light of a combination of the references. Thus Applicants respectfully request that the Examiner withdraw the rejection and issue a Notice of Allowance for this application.

Respectfully submitted,



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